Using hiPSC-derived lung organoids, a clinically-relevant system, to validate & winnow a list of approved drugs that inhibit SARS-CoV-2 cytopathy

Grant Award Details

Using hiPSC-derived lung organoids, a clinically-relevant system, to validate & winnow a list of approved drugs that inhibit SARS-CoV-2 cytopathy

Grant Type: Discovery Research Projects

Grant Number: DISC2COVID19-12022

Project Objective: Establish pluripotent stem cell based lung organoid system to emulate that in vivo conditions for SARS-CoV-2 infection and identify extant drugs that are effective in the patient representative platform.

Investigator:

Name:	Evan Snyder
Institution:	Sanford Burnham Prebys Medical Discovery Institute
Type:	PI

Disease Focus: COVID-19, Infectious Disease, Respiratory Disorders

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $228,229

Status: Active

Grant Application Details

Application Title: Using hiPSC-derived lung organoids, a clinically-relevant system, to validate & winnow a list of approved drugs that inhibit SARS-CoV-2 cytopathy

Public Abstract:

Research Objective

Using authentic in vitro models of the human lung, complete with inflammatory cells & vessels, we will validate drugs that might be rapidly repurposed for use in patients with COVID-19.

Impact

The impact will be the avoidance of an animal model once an approved medication hit has been verified by our model. The medication can then be immediately used in a clinical trial.

Major Proposed Activities

- hiPSC-derived lung organoid development & baseline cellular characterization from a diverse group of patients (race, gender, HLA type).
- Molecular characterization of the above-mentioned organoids that are also invested with isogenic alveolar macrophages & vasculature.
- Infect above organoids with pseudovirus & complete SARS-CoV-2 & characterize cellular, genomic, & proteomic changes from baseline.
- Determine impact of the narrow-spectrum oral clinical-stage protease inhibitor ONO5344 on "rescuing" infected organoids.
- Determine impact of the broad-spectrum oral late-stage protease inhibitor VBY825 on "rescuing" infected organoids.
- If 1 or both drugs are effective in this clinically-relevant system, send INTERACT, pre-IND, and/or IND packages to the FDA to expedite redesignation & advancement to clinical trials.

Statement of Benefit to California:

This research will benefit Californians by using authentic "mini-human lungs-in-a-dish" to test drugs that already exist & are often being used for other purposes by patients but which must be validated for effiacy against SARS-CoV-2. Until a vaccine is available, a drug that suppresses the severity & contagion of COVID-19 might be the next best thing. If we can bypass animal testing with this system (no good COVID-19 animal model yet exists), we might fast-track these drugs to patients.

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